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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,037	12/31/2001	Avigdor Levanon	10793/44	8494

26646 7590 10/20/2004

KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,037	LEVANON ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-163* is/are pending in the application.

4a) Of the above claim(s) *17-152,155 and 158-163* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,153,154,156 and 157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/27/03+ 8/6/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *attachment*.

DETAILED ACTION

1. Acknowledgment is made of applicant's election with traverse of Group IX drawn to epitopes. The traversal is on the grounds that the restriction is improper as applicant contends that Groups I, II III. IV and IX can be examined with together without serious burden on the examiner. This has been considered but not found persuasive. Groups I, II, III and IV are drawn to antibodies. Group IX is drawn to polynucleotides encoding epitopes and the instant elected group is drawn to epitopes. Each of these products differ structurally and are made by different methods and have different uses and are recognized as separate and unique in the art as evidenced by the different U.S. classification. The examination of and epitope, and antibody and polynucleotides would not be co-extensive and therefore burdensome, and thus restriction for examination purpose is proper and adhered to. The restriction requirement is therefore made final.

2. The examiner acknowledges applicant's observation that Group II seems to be in error as it encompasses the instant claims by virtue of a typographic error which set forth claims 1-31, 34-9, 51, 52, 61, 68-72, 74, 76-80, 82-86, 87, 96, 103-107, 109, 11-115, 117, 118 and 155 as group II rather than 19-31, 34-49, 51, 52, 61, 68-72, 74, 76-80, 82-86, 87, 96, 103-107, 109, 11-115, 117, 118 and 155.

3. Claims 1-163 are pending. Claims 17-152, 155 and 158-163, drawn to non-elected inventions, are withdrawn form consideration. Claims 1-16, 153, 154, 156 and 157 are examined on the merits.

Priority

4. Acknowledgement is made of applicant's claim to an earlier effective priority date via provisional application 60/258,948. However, said provisional application, although providing a written description of antibodies comprising a first hypervariable region comprising SEQ ID NO:8, does not provide any description of the genus of epitopes claimed, or the specific ligand of the phagemid clone Y1 which comprises SEQ ID NO:8. The provisional application states that Y1 binds to many leukemia cells but does not bind to the corresponding normal hematopoietic cell (page 96, lines 15-17, page 100, paragraph 8.4, and page 105, Table 11). Accordingly,

claims 1-16, 153, 154, 156 and 157 are given the effective priority date of the instant filing on December 31, 2001.

Claim Objections

5. Claim 156 is objected to for failing to comply with the Sequence Rules. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 5 recite "P is (A)m(A)n(X)u or (X)u(A)n(A)m or (A)n(X)u(A)m or (A)n(A)m(X)u or (X)u(A)m(A)n or (A)m(X)u(A)n", wherein A is any negatively charged amino acid or L, I, P, F, S or G. It is unclear if the content of "(A)" must be identical for (A)m and (A)n or if the content of "(A)" can be independently selected from any negatively charged amino acid or L, I, P, F, S or G. For purpose of examination, both alternatives will be considered.

Claims 1 and 5 recite a formula comprising (W)z-P-(Y*)t-P, wherein *=(S)r. It is unclear if the content of both "P"s must be identical or independently selected. For purpose of examination, both alternatives will be considered.

Claims 1, 5 and 9 recite "wherein the isolated epitome is capable of being bound by an antibody, antigen-binding fragment thereof, or complex thereof comprising at least one antibody or binding fragment thereof comprising a first hypervariable region comprising SEQ ID NO:8". It is unclear if the first recitation of "antibody" and the antigen-binding fragment thereof carries the limitation of comprising the "first hypervariable region comprising SEQ ID NO:8". For purpose of examination, said limitation of comprising the "first hypervariable region comprising

SEQ ID NO:8" will be applied to the last recited limitation in the Markush group, that of "the complex thereof".

Claims 3 and 7 recite "A is Glutamate, gamma carboxyl Glutamate or Aspartate". It is unclear if all of the A included in (A)m and (A)n must be Glu, g-Glu or Asp or if only a single A need be Glu, g-Glu or Asp. For purpose of examination, the limitation will be applied to both alternatives.

Claim 7 recites "Y is a peptide conjugate of Tyrosine or a glyco conjugate of Asparagine, Serine or Threonine". Claim 8 recites "Y is a peptide conjugate of Tyrosine". It is unclear if all of the "Y"s in claim 5 are limited by the dependent claims 7 and 8, or if only one Y in claim 5 is so limited. For purpose of examination, all alternatives will be considered.

Claim 9 is vague and indefinite in the recitation of "X is any amino acid except the above". It is unclear if "the above" refers to what is immediately above, such as the "sulfated molecule" or if "X" refers to the "the above" collectively to exclude G, E, D Y and "the sulfated molecule".

Claim 15 recites "capable of improving the binding capacity of the epitome" but fails to state to what the epitome is binding.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-8 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies which bind to epitopes wherein said eptiope comprises Y =Tyr, Asp, Ser or Thr as a naturally occurring molecule capable of being sulfated, does not reasonably provide enablement for antibodies which bind to epitopes wherein said eptiope comprises Y= lipid, carbohydrate, peptide, glycolipid, glycoprotein, lipoprotein, LPS or any other molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The art teaches that a consensus sequence is needed for the action of enzymes responsible for the post-translational sulfation of protein molecules. The interruption of the claimed formulas by Y groups which are larger than an amino acid would necessarily disrupt the binding to the active site of the sulfating enzyme. The art is consistent with the direct binding of the hydroxyl group of tyrosine with the sulfate group within the active site of the tyrosyl protein sulfotransferase (Kehoe et al, Chemistry and Biology, 2000, Vol. 7, R57-R61, reference of the IDS filed January 27, 2003). It is unclear how the remainder of the consensus sequence as claimed would interact within the active site of the sulfotransferase when spatially distanced from the atom which is binding to the active site sulfate, as in the case of the lipids, carbohydrates, peptides, glycopeptides, glycoproteins, lipoproteins and lipopolysaccharides claimed which when present as the indicated "Y" group would necessarily distance the other atoms of the consensus sequence, such as (W)z and P. Further, there is no support in the specification or any art of record to indicate that the surrounding sequence given in formulas I and II would govern the sulfation of non-amino acid molecules such as lipid, carbohydrate, glycolipid, LPS or any other molecule, or that the resulting molecule comprising the indicated formulas would bind to an antibody comprising a first hypervariable region comprising SEQ ID NO:8. It is noted that Kehoe et al teach 13 sequences which are known to be sulfated on tyrosine (Table 1), and other amino acid sequences which become tyrosine sulfated when attached to a carrier protein (table 2), no indication is given which would support the notion that insertion of a lipid, carbohydrate, glycolipid, LPS or any other molecule in place of the sulfated tryosine(s) would result in increase sulfation of the lipids, carbohydrates, peptides, glycopeptides, glycoproteins, lipoproteins and lipopolysaccharides relative to the sulfation of the same lipids, carbohydrates, peptides, glycopeptides, glycoproteins, lipoproteins and lipopolysaccharides without the surrounding consensus sequence of (W)z-P-(Y)t-P.

10. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claim 12 is drawn to a homolog or mimetic of the isolated epitome of any one of claims 1-10. The specification teaches the consensus sequence for sulfation requires Formula I, II or III. The specification does not teach how to make homologs or mimetics which would not be encompassed by the instant Formula I, II or III. Further, when given the broadest reasonable interpretation, the term "mimetic" is not limited to protein sequences, but can encompass non-protein organic molecules. The specification does not set forth a nexus between the structure of an epitome of a homolog and the structure of the instant sequence motif. A requirement of 35 U.S.C. 112, is that one of skill in the art can make the claimed product without undue experimentation. It is noted that isolation by screening methods of homologs or mimetic which would read on the instant claim does not satisfy the requirement of how to make the claimed homologs and mimetics because making the claimed homologs and mimetic would require a prior knowledge of their sequence; thus, the task of first isolating the claimed homologs and mimetics prior to acquiring the sequences thereof constitutes undue experimentation. Given the lack of teachings in the specification regarding the structural requirements for homologs or mimetics which are not limited by the instant Formulas, one of skill in the art would be subject to undue experimentation in order to make and use the broadly claimed invention.

11. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 12 is drawn to a genus of homologs and a genus of mimetics each of which comprise members having structural and function deviations from the epitopes comprised within Formula I, II and III. Thus the genus of homologs and the genus of mimetics are both highly variant as set genuses comprise members which vary from the structural requirements of Formulas I, II and III. The genuses also encompass members which differ widely in function from the members possessing Formulas I, II and III. It is noted that the requirement of binding to an antibody or an antigen-binding fragment thereof does not serve to limit the function of the genus of homologs and mimetics claimed because any peptide can bind to an antibody and an antibody can be raised to a small non-protein molecule when said molecule is conjugated to a

larger protein. The disclosure of the motifs of Formula I, II and III does not adequately describe the genuses of homologs and mimetics because each genus encompasses members which vary widely in structure and function from those members which possess the motifs of Formula I, II or III. One of skill in the art would reasonably conclude that applicant was not in possession of the claimed genuses at the time of filing..

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1, 2, 5, 6 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Mosesson et al (WO 98/12318, 03-1998).

Mossesson et al disclose

(i) a peptide comprising the sequence HPAETEYESLYP (Registry No. 204975-91-7) wherein the sequence comprises the instant W=Ala, A-X-A, sulfo-Tyr, A-A-X, as evidenced by the attached Registry No. sequence, wherein the content of both "P" and "A" is chosen independently, thus anticipating claim 1; and also anticipating claim 5, wherein (Y)r has r=0 and wherein W=His, P(first)=Pro-Ala, P(second)=Glu-Thr-Glu, (Y)t=sulfo-Tyr, P(third)=Glu-Ser-Leu, (Y)t=sulfo-Tyro and P(fourth)=Pro;

(ii) a peptide comprising the sequence HPAETEYESLYPEDD (Registry No. 204975-94-0), wherein the sequence comprises the instant W=Ala, A-X-A, sulfo-Tyr, A-X-A, as evidenced by the attached Registry No. sequence, wherein the content of both "P" and "A" is chosen

independently, and wherein the last occurring A=D and m or n for said A equals 2; and also anticipating claim 5, wherein (Y)r has r=0 and wherein W=His, P(first)=Pro-Ala, P(second)=Glu-Thr-Glu, (Y)t=sulfo-Tyr, P(third)=Glu-Ser-Leu, (Y)t=sulfo-Tyro and P(fourth)=Pro-Glu-Asp-Asp, wherein m or n =2 for the final (A) group;

(iii) a peptide comprising the sequence AETEFESLYPEDD (Registry No. 204975-95-1), wherein the sequence comprises the instant W=Ala, A-X-A, sulfo-Tyr, A-X-A, as evidenced by the attached Registry No. sequence, wherein the content of both "P" and "A" is chosen independently, and wherein the last occurring A=D and m or n for said A equals 2;

(iv) a peptide comprising the sequence HPAEVEYEALYPEDD (Registry No. 204975-97-3), wherein the sequence comprises the instant W=Ala, A-X-A, sulfo-Tyr, A-X-A, sulfo-Tyr, X-A-A, as evidenced by the attached Registry No. sequence, wherein the content of both "P" and "A" is chosen independently, and wherein the last occurring A=D and m or n for said A equals 2; and also anticipating claim 5, wherein (Y)r has r=0 and wherein W=His, P(first)=Pro-Ala, P(second)=Glu-Thr-Glu, (Y)t=sulfo-Tyr, P(third)=Glu-Ala-Leu, (Y)t=sulfo-Tyro and P(fourth)=Pro-Glu-Asp-Asp, wherein m or n =2 for the final (A) group;

(v) a peptide comprising the sequence AETEYESLYPEDD (Registry No. 204975-96-2) wherein the sequence comprises the instant W=Ala, A-X-A, sulfo-Tyr, A-X-A, sulfo-Tyr, X-A-A, as evidenced by the attached Registry No. sequence, wherein the content of both "P" and "A" is chosen independently, and wherein the last occurring A=D and m or n for said A equals 2;

(vi) a peptide comprising the sequence AEVEYEALYPEDD (Registry No. 204976-00-1 and Registry No. 204976-03-4) wherein the sequence comprises the instant W=Ala, P(first)=Glu, P(second)=Val-Glu, sulfo-Tyr, P(third)=Glu-Ala-Leu, sulfo-Tyr, P(fourth)=Pro-Glu-Asp-Asp, wherein the content of both "P" and "A" is chosen independently, and wherein the last occurring A=D and m or n for said A equals 2;

(vii) a peptide comprising the sequence EALYPEDD (Registry No. 204976-02-3), wherein the sequence comprises W=0 by virtue of z=0, P=A-X-A, sulfo-Tyr, X-A-A, wherein the content of both "P" and "A" is chosen independently, and wherein the last occurring A=D and m or n for said A equals 2, thus fulfilling the specific embodiments of claim 1;

The disclosed peptides fulfill the specific embodiments of claims 1 and 5 with regard to being capable of binding to an antibody or an antigen-binding fragment thereof, because all peptides are thus capable. It is noted that the limitation of binding to an antibody or antigen binding fragment thereof comprising SEQ ID NO:8 is not applied to the entirety of the claims because of the broadest reasonable interpretation of the claims as set forth under the rejection under 112, second paragraph above. The sulfo-Tyr fulfills the specific embodiment of claim 6 drawn to a peptido conjugate as the sulfo-Tyr moiety is a peptido conjugate. Mossesson et al disclose compositions comprising said peptides (page X, lines Y-Z) thus fulfilling the specific embodiment of claim 14. Claims 15 and 16 are included with this rejection because it is unclear what the epitome is binding to.

14. Claims 1, 2 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Muramatsu et al (Peptide Chemistry, 1995, Vol. 32, pp. 297-300).

Muramastsu et al disclose a peptide comprising the sequence FEEIPYYYLQ (Registry No. 165598-24-3), wherein the instant W=F, P=(A)n(A)mX, wherein (A)n is Glu-Glu, (A)m is Ile and X is Pro, wherein t=3 and (Y)t is sulfo-Tyr-sulfo-Tyr-sulfo-Tyr and wherein P=(A)n(A)m(X)u, wherein m=0 and u=1 and wherein n and u=1, A=L and X=Gln. It is noted that the limitation of binding to an antibody or antigen binding fragment thereof comprising SEQ ID NO:8 is not applied to the entirety of the claims because of the broadest reasonable interpretation of the claims as set forth under the rejection under 112, second paragraph above. The sulfo-Tyr fulfills the specific embodiment of claim 2 drawn to a peptido conjugate as the sulfo-Tyr moiety is a peptido conjugate. Mossesson et al disclose compositions comprising said peptides (page 299,Table 1) thus fulfilling the specific embodiment of claim 14. Claims 15 and 16 are included with this rejection because it is unclear what the epitome is binding to.

15. Claims 1-3 and 14-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Hubbell et al (US 20030064410, priority to 60/306,726, filed July 20, 2001).

Hubbell et al disclose

(a) the peptide comprising the sequence VFVSSVVSS (Registry No. 491841-54-4), wherein W=Val, P=(A)n(A)m(X)u, wherein m=0 and n and u=1, wherein (A)n=Phe and (X)u=Val,

wherein t=2 and (Y)2=sulfo-Ser-Sulfo-Ser, wherein u and m=2, and n=0, wherein P=(X)u(A)m(A)n is Val-Val-Ser-Ser. It is noted that the limitation of binding to an antibody or antigen binding fragment thereof comprising SEQ ID NO:8 is not applied to the entirety of the claims because of the broadest reasonable interpretation of the claims as set forth under the rejection under 112, second paragraph above. The sulfo-Tyr fulfills the specific embodiment of claim 2 drawn to a peptido conjugate as the sulfo-Ser moiety is a peptido conjugate. Mossesson et al disclose compositions comprising said peptides (page X, lines Y-Z) thus fulfilling the specific embodiment of claim 14. Claims 15 and 16 are included with this rejection because it is unclear what the epitome is binding to; and

(b) the peptide comprising the sequence GGYDYG (Registry No. 491841-60-2), wherein W=Gly, P=(A)n(A)m(X)u, wherein m and u=0 and (A)n=G, sulfo-Tyr, P=(A)n(A)m(X)u, wherein m and u=0 and (A)n=Asp.

It is noted that the limitation of binding to an antibody or antigen binding fragment thereof comprising SEQ ID NO:8 is not applied to the entirety of the claims because of the broadest reasonable interpretation of the claims as set forth under the rejection under 112, second paragraph above. Hubbell et al disclose compositions comprising said peptides (page X, lines Y-Z) thus fulfilling the specific embodiment of claim 14. Claims 15 and 16 are included with this rejection because it is unclear what the epitome is binding to. The peptide of section (b) above, fulfills the specific embodiment of claim 3 because W=Gly and (A)n=Asp.

16. Claims 1-3, 5, 6, 14-16, 153, 154, 156 and 157 are rejected under 35 U.S.C. 102(b) as being anticipated by Ward et al (Biochemistry, 1996, Vol. 35, pp. 4929-4938, reference #70 of the IDS filed January 27, 2003).

Claim 153 is drawn to an isolated epitome comprising GPIbalpha amino acid sequence Tyr276 to Glu282, wherein at least one of amino acids 276, 278 and 279 is sulfated. Claim 154 embodies the epitome of claim 153, further comprising residues 283-285 of GPIbalpha. Claim 156 is drawn to an isolated GPIbalpha N-terminal peptide having an apparent molecular weight of about 40 Kda, said peptide comprising the epitome YDYYPEE, wherein at least one tyrosine residue within said epitome is sulfated. Claim 157 is drawn to an isolated peptide consisting of

amino acids 1-282 of GPIbalpha, wherein at least one of amino acids 276, 278 and 279 is sulfated.

Ward et al disclose an isolated epitome comprising amino acid sequence Tyr276 to Glu282 of GPIbalpha (lines 14-16 of abstract) wherein at least one tyrosine residue is sulfated, this peptide also metes the specific embodiment of claim 156 which specifies the sequence YDYYPEE; an isolated epitome comprising amino acid sequence Tyr276 to Glu282 and further comprising residues 283-285 (page 4935, first column, lines 15-21) because Ward et al disclose the peptide consisting of residues 1-282 of GPIbalpha (page 4934, first column, line 12). It would be inherent in the peptide of residues 1-282 of GPIbalpha that at least one of amino acids 276, 278 and 279 is sulfated because the peptide comprises the sequence YDYYPEE which was disclosed by Ward et al to be 90% sulfated on Tyr 278 and 279 and 50% sulfated on Tyr 282. Ward et al disclose the peptide of DEGDTDLYDYYPEEDTEGD (page 4930, first column, line 44) which fulfills the specific embodiments of claims 5 and 6 with (Y)r=0, because z=1, (W)z=Gly, P(first)=Asp-Thr-Asp as (A)n(X)u(A), P(second)=Leu as (A)n, wherein m and u=0, sulfo-Try, P(third) as (A)n=Asp, wherein m and u=0, t=2 and (Y)t=sulfo-Try-sulfo-Tyr, P(forth)=Pro-Glu-Glu-Asp as (X)u(A)n(A)m, wherein u and m=1 and n=2 and (X)u=Pro, (A)n=Glu and (A)m is Asp. Said epitome also fulfills the specific embodiment of claims 1-3 wherein z=0, P(first)=(A)n(X)u(A)m, wherein, n=u=m=1 and wherein (A)n=Asp, (X)u=Thr and (A)m=Asp; t=1 and (Y)t=sulfo-Try; and wherein P(second)=(A)m(A)n(X)u, wherein n and u are 0 and wherein (A)m is Asp. The claims also fulfill the specific embodiments of claim 3 because W is Gly, Y is sulfo-Tyrosine, one "A" is Asp, and q is 1.

17. Claims 1, 2, 5, 6, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Leppanen et al (Journal of Biological Chemistry, 1999, Vol. 274, pp. 24838-24848)

Claim 13 embodies the epitome of any of claims 1-10 wherein the isolated epitome comprises at least one post-translational modification in addition to sulfation.

Leppanen et al disclose the glycosulfopeptide-6 (GSP-6, page 24840, Figure 2) having the sequence GQATE-sulfo-Tyr-E-sulfo-Tyr-LD-sulfo-Tyr-DFLPETEPPEML having a sialyl Lewis carbohydrate motif on the Threonine of residue 57, thus fulfilling the specific embodiment of claim 13 specifying an additional post-translational modification. The disclosed peptide

sequence fulfills the specific embodiments of claims 1 and 5 having W=Ala, X-A=Thr-Glu, sulfo-Tyr, A=Glu, sulfo-Tyr, AA=Leu-Asp-sulfo-Tyr, AAX=Asp-Phe-Leu to anticipate claim 5, or W=Leu, A=Asp-sulfo-Tyr, A=Asp to anticipate claim 1. It is noted that Leppanen et al disclose that core 2-based sialyl Lewis X O-glycan at position 57 coffers high-affinity binding of the peptide to P-selectin which would meet the limitation of claim 15.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Panet et al (WO 98/39469, 09-1998).

Panet disclose SEQ ID NO:8 as isolated from a synthetic human antibody library (page 14, lines 35-37 and page 74, line 13 to page 76, line 19). SEQ ID NO:8 is IG-NC-650 of Panet et al. Panet et al disclose that IG-NC-650 was isolated by panning for antibodies which bound to Namalwa cells transfected with CD44V3-10. Thus, it is obvious that CD44V3-10 as expressed in Namalwa cells comprises the epitome of claim 1, because the antigen-binding fragment of SEQ ID NO:8 binds to an epitome on CD44V3-10 as expressed by Namalwa cells.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
9/7/2004

KAREN A. CANELLA PH.D
PRIMARY EXAMINER

KAREN A. CANELLA PH.D
PRIMARY EXAMINER

ATTACHMENT TO
paper 20040907

L33 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:197609 CAPLUS
DOCUMENT NUMBER: 128:241252
TITLE: Thrombin inhibition by human **fibrinogen** . **gamma.**' chain peptides
INVENTOR(S): Mosesson, Michael W.; Meh, David A.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812318	A1	19980326	WO 1997-US10429	19970613
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5985833	A	19991116	US 1996-713885	19960917
AU 9733966	A1	19980414	AU 1997-33966	19970613
PRIORITY APPLN. INFO.:			US 1996-713885 A	19960917
			WO 1997-US10429 W	19970613

IT **204975-91-7 204975-92-8 204975-94-0**
204975-95-1 204975-96-2 204975-97-3
204975-99-5 204976-00-1 204976-01-2
204976-02-3 204976-03-4 204976-04-5
204976-05-6 204976-06-7 204976-07-8
204976-09-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thrombin inhibition by human **fibrinogen** γ ' chain peptides)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **204975-94-0** REGISTRY
CN L-Leucine, L-α-glutamyl-L-histidyl-L-prolyl-L-alanyl-L-α-glutamyl-L-threonyl-L-α-glutamyl-O-sulfo-L-tyrosyl-L-α-glutamyl-L-seryl-L-leucyl-O-sulfo-L-tyrosyl-L-prolyl-L-α-glutamyl-L-α-aspartyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **17**
NTE **modified**

type	------ location ------		description
modification	Tyr-8	-	sulfo<SO3H>
modification	Tyr-12	-	sulfo<SO3H>

SEQ 1 EHPAETEYES LYPEDDL
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HITS AT: 4-13
MF C89 H125 N19 O42 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

L38 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **204975-95-1** REGISTRY
CN L-Leucine, L-α-glutamyl-L-histidyl-L-prolyl-L-alanyl-L-α-glutamyl-L-threonyl-L-α-glutamyl-L-phenylalanyl-L-α-glutamyl-L-seryl-L-leucyl-O-sulfo-L-tyrosyl-L-prolyl-L-α-glutamyl-L-α-aspartyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **17**
NTE **modified**

type	------ location ------		description
modification	Tyr-12	-	sulfo<SO3H>

SEQ 1 EHPAETEFES LYPEDDL
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HITS AT: 4-13
MF C89 H125 N19 O38 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

L39 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **204975-96-2** REGISTRY
CN L-Leucine, L-alanyl-L-α-glutamyl-L-threonyl-L-α-glutamyl-O-sulfo-L-tyrosyl-L-α-glutamyl-L-seryl-L-leucyl-O-sulfo-L-tyrosyl-L-prolyl-L-α-glutamyl-L-α-aspartyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **14**
NTE **modified**

type	------ location ------		description
modification	Tyr-5	-	sulfo<SO3H>
modification	Tyr-9	-	sulfo<SO3H>

SEQ 1 AETEYESLYP EDDL
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HITS AT: 1-10
MF C73 H104 N14 O37 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

L42 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **204976-00-1** REGISTRY
CN L-Leucine, L-alanyl-L-α-glutamyl-L-valyl-L-α-glutamyl-O-sulfo-L-tyrosyl-L-α-glutamyl-L-alanyl-L-leucyl-O-sulfo-L-tyrosyl-L-prolyl-L-α-glutamyl-L-α-aspartyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **14**
NTE **modified**

type	location		description
modification	Tyr-5	-	sulfo<SO3H>
modification	Tyr-9	-	sulfo<SO3H>

SEQ 1 AEVEYEALYP EDDL
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HITS AT: 3-10
MF C74 H106 N14 O35 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

L44 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **204976-02-3** REGISTRY
CN L-Leucine, L-α-glutamyl-L-alanyl-L-leucyl-O-sulfo-L-tyrosyl-L-prolyl-L-α-glutamyl-L-α-aspartyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **9**
NTE **modified**

type	------ location ------		description
modification	Tyr-4	-	sulfo<SO3H>

SEQ 1 EALYPEDDL
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HITS AT: 2-5
MF C47 H69 N9 O22 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

L29 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:624533 CAPLUS
DOCUMENT NUMBER: 123:102010
TITLE: Structure/activity relationships of hirudin peptides containing sulfated tyrosine residues
AUTHOR(S): Muramatsu, Ryo; Komatsu, Yasuhiko; Nukui, Eriko; Okayama, Toru; Morikawa, Tadanori; Kobashi, Kyoichi; Hayashi, Hideya
CORPORATE SOURCE: Pharmaceuticals and Biotechnology Laboratory, Japan Energy Corporation, Saitama, 335, Japan
SOURCE: Peptide Chemistry (1995), Volume Date 1994, 32nd, 297-300
CODEN: PECHDP; ISSN: 0388-3698
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **146843-37-0 146843-38-1 146843-39-2 165598-24-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-activity relationships of hirudin peptides containing sulfated tyrosine residues for antithrombotic and platelet aggregation inhibiting activities)

L43 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **165598-24-3** REGISTRY
CN L-Glutamine, N2-[N-[N-[N-[1-[N-[N-[N-[N-(N-glycyl-L-α-aspartyl)-L-phenylalanyl]-L-α-glutamyl]-L-α-glutamyl]-L-isoleucyl]-L-prolyl]-O-sulfo-L-tyrosyl]-O-sulfo-L-tyrosyl]-O-sulfo-L-tyrosyl]-L-leucyl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 12
NTE modified (modifications unspecified)

type	------ location ------		description
modification	Tyr-8	-	sulfo<SO3H>
modification	Tyr-9	-	sulfo<SO3H>
modification	Tyr-10	-	sulfo<SO3H>

SEQ 1 GDFEEIPYYY LQ
=====
HITS AT: 6-11

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C74 H97 N13 O32 S3
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Prep
PRP (Properties); USES (Uses)

Absolute stereochemistry.